IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Chien, Te-Yen

Confirmation No.: **1537**

Application No.: **10/621,711**

Group Art Unit: **1615**

Filing Date: **July 17, 2003**

Examiner: **Ghali, Isis A.D.**

For: **Transdermal Hormone Delivery System: Compositions and Methods**

DECLARATION OF THOMAS M. ROSSI PURSUANT TO 37 C.F.R. §1.132

I, Thomas M. Rossi, declare as follows.

1. I am a United States citizen residing at 104 Sandy Ridge Mount Airy Road, Stockton, New Jersey.

2. I received a Bachelor's degree in Chemistry in 1980 from the Western Connecticut State University, and Ph.D. degree in Analytical Chemistry in 1985 from Texas A&M University, as set forth in my professional resume attached hereto.

3. From 1985 to 1991, I was employed with SmithKline Beecham, Inc., in numerous positions leading to Assistant Director, Pharmaceutical Analysis. From 1991 to 2003, I was employed with Johnson & Johnson Company in several leadership positions, including Assistant/Senior Director of Analytical Chemistry (1991-1996), Vice President Global Chemical, Pharmaceutical and Preclinical Development (1996-2000), Senior Vice President, Process Excellence and Global Change Management (2000-2002) and Senior Vice President in Drug Safety and Surveillance (2002-2003). From 2003 to the present I have served as Managing Member of R&D Excellence, Inc., a consulting company offering Services in R&D strategy, operational improvement and technical development. Additional details of my professional history are set forth in my professional resume.

4. From 2004 to the present I have served as President and Chief Executive Officer of Agile Therapeutics, Inc., an early stage pharmaceutical company developing transdermal hormone delivery devices.

5. I have had over twenty-five years of scientific training and business experience in the pharmaceutical industry, including operations assessments and start-ups, mergers and acquisitions, product line extensions, general management, board level partnering and regulatory compliance. I am the author, co-author or presenter of numerous publications, invited reviews and invited lectures in these fields. I am or have been a member of several scientific or business committees and advisory boards, including the Sino American Pharmaceutical Association (honorary advisor 1998-present), Pharmaceutical Research Manufacturer's Association, Analytical R&D Steering Committee (1995-1996), American Association of Pharmaceutical Scientists (since 1985) with service on the Public Policy Committee (1994-1997), American Chemical Society (since 1980), elected to Philadelphia Section Board of Directors (1986), and participation on Continuing Education Subcommittee (1986-1990, chaired 1989-1990). I served as Adjunct Assistant Professor of Pharmaceutical Chemistry at the University of Kansas from 1989-1992.

6. As mentioned, I am President and Chief Executive Office of Agile Therapeutics, Inc., licensee and developer of the technology disclosed and claimed the above-referenced U.S. Patent Application Serial No. 10/621,711, entitled "Transdermal Hormone Delivery System: Compositions and Methods" (referred to hereinafter as "the present application"), the claims of which are currently under rejection in the U.S. Patent and Trademark Office.

7. I have read and am familiar with the Official Action dated August 4, 2006 in the present application. I understand the nature of the rejections made by the examiner concerning alleged obviousness of the claimed invention over the teachings of U.S. Patent 5,876,746 ("the 746 patent") in view of U.S. Patent 5,023,084 ("the 084 patent") and, for some claims, additionally in view of U.S. Patent 5, 876,746 ("the 746 patent"). According to the examiner, it would have been obvious to provide a transdermal delivery device to deliver combined estrogen and progestin in a matrix comprising a combination of enhancers as disclosed by the 956 patent, and to add capric acid as disclosed by the 084 patent for a different type of transdermal device, motivated by the teaching of the 084 patent that capric acid provides satisfactory skin absorption enhancement in that different system; therefore a

four-component enhancer combination comprising DMSO, lauryl lactate, ethyl lactate and capric acid would be expected to deliver the hormonal combination to the skin of the user at a satisfactory enhanced rate.

8. I strongly disagree that the teachings of the aforementioned patents would have rendered obvious the transdermal delivery system claimed in the present application. The transdermal system disclosed in the 956 patent is similar to the system disclosed and claimed in the present application, except that the adhesive polymer matrix of the 956 patent utilizes a three-component permeation enhancer combination, while the present application claims a system in which the adhesive polymer matrix contains a four-component enhancer combination (capric acid added). Yet in clinical trials, the steady state serum concentration of progestin delivered by a 10 or 20 cm^2 patch of the present invention was remarkably better than that of the 956 patent's formulation – about 1500-3000 pg/ml for the presently claimed formulation (Table 2 of the present application), versus only about 500 pg/ml on average for the 956 patent's formulation (Fig. 4 of 956 patent, see "Group B" (2 x 10 cm^2 patches). As explained fully in the Declaration of Agis Kydonieus, this remarkable improvement in *in vivo* progestin delivery by re-formulating the matrix to include capric acid could not have been predicted from the mere knowledge (as taught in the 084 patent and elsewhere in the literature) that capric acid is a good skin permeation enhancer for hormone delivery.

9. In my opinion, the low level of *in vivo* transdermal progestin delivery afforded by the 956 patent's formulation is not sufficient for commercial development of a transdermal contraceptive device. In contrast, the transdermal delivery system of the present invention enables delivery of robust amounts of contraceptive hormones, especially progestins. For this reason, Agile Therapeutics has taken a license to the intellectual property and has been actively developing a transdermal contraceptive delivery system for commercial sale.

10. It should be noted that Agile Therapeutics was formed specifically with the intention of commercializing a product or product(s) derived from the inventions described in the present application. Since its inception, the company and its predecessor organization have raised a total of $ 31.5 million. The company is run by an experienced management team and funded by high quality private equity investors with experience in health care product development and commercialization. These funds have been dedicated to product development activities based on the invention of the present application. The company

reviewed the 084 and 956 patents for commercial potential, and, although the rights to those patents were available to the company, only the technology described in the present application was selected for commercial development.

11. In sum, then, the excellent *in vivo* performance of the transdermal system of the present invention has enabled and encouraged commercial development of the system for contraception, whereas systems described in the 956 patent and the 084 patent were not selected for development. This technology has enjoyed significant commercial success, attracting sufficient interest to form a company dedicated to its development, and several million dollars of investment to date.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the above-referenced application or any patent issued thereon.

2 NOV 2006
DATE

THOMAS M. ROSSI, PH.D.

Thomas M. Rossi, Ph.D.

104 Sandy Ridge Mount Airy Rd.
Stockton, New Jersey 08559
thomasrossi@comcast.net Res: (609) 397-4916 Bus: (609) 397-5860

EXECUTIVE PROFILE

RESEARCH & DEVELOPMENT - PROCESS / BUSINESS MANAGEMENT

Senior level experience with Johnson & Johnson focused on Building/Managing Technical Organizations, Product Development/Commercialization, Organization/Business Transition and Six-Sigma Process Excellence Integration. Leadership roles in Company Business Planning, Global Programs/Projects and Development of High Performance Environments. Additional expertise in:

- Business Mergers/Acquisitions
- Operations Assessment/Start-Ups
- Product Line Extensions
- General Management
- Board Level Partnering
- Regulatory Compliance

EXPERIENCE

Agile Therapeutics, Inc., West Conshohocken PA | May 2004 to present

President and CEO

Assumed leadership of this early stage pharmaceutical development company, raised $4.5MM in venture capital investment, strengthened management team and set new direction for product development success.

R&D Excellence, LLC, Stockton NJ | 2003 to present

Managing Member

Founder and managing member of a consulting company offering services in R&D Strategy, Operational Improvement, and Technical Development.

Co-founder and director of SansRosa Pharmaceutical Development, Inc.

Start up pharmaceutical development company focused on the development of a generation of novel products for the treatment of rosacea. Oversaw early start up, establishing intellectual property, market opportunity forecast, and scientific direction. Recruited management team & identified funding sources.

Johnson & Johnson PRD, Raritan, NJ | 1991 to 2003
(merged entity of Janssen & PRI Research)

***Senior Vice President in Drug Safety and Surveillance** (May 2002 - March 2003)*

Reporting to the Executive Vice President of Drug Safety and Post Marketing Medical Assessment, led a process, organization, and IT system redesign project in support of the Group Operating Committee

- *Successfully brought together and gave direction to a team of senior executives charged with improving the compliance and proactive safety risk management*

capability of the company.
- *Achieved all milestones for this mission critical project*
- *Improved clarity of legal accountability for drug safety activities across multiple J&J operating companies*
- *Improved performance of core processes for drug safety*

Senior Vice President, Process Excellence and Global Change Management *(2000-May 2002)*
Asked by Company Group Chairman to lead a team of senior executives charged with steering the merger of two major internal Pharmaceutical R&D units to form J&J PRD, a 3500 employee, transnational Pharmaceutical R&D unit. Additionally asked to introduce Process Excellence.

Member of the Board, responsible for all internal merger and Process Excellence activity.

- Achieved total success of the merger and the Process Excellence start-up with the sincere appreciation of Corporate and Company Management.

- Upon completion of the merger, established 6-sigma based Process Excellence in the R&D organization as the standard methodology for achieving continuous improvement and created a small department to serve as an internal consulting group.

- As a member of the R&D senior leadership team, supported colleagues in developing strategic direction for the new organization, developing performance metrics and selecting and executing process improvement projects.

- Delivered a significant reduction in phase III cycle time, and established a firm Process Excellence foundation for continued improvements.

Vice President Global Chemical, Pharmaceutical and Preclinical Development *(1996-2000)*
Joined the RWJ PRI Management Board as the head of Chemical and Pharmaceutical Development and led the division through a change in operating model to create a strong team centered approach to R&D and to reduce management layers. In 1998 my responsibilities were expanded to include oversight of Toxicology and Drug Metabolism. The entire division was comprised of approximately 400 scientists in the US and Switzerland with an annual budget of approximately $200MM.

- The Department successfully delivered on all its milestone commitments for investigational drugs, line extensions, and commercialization of products including: Evra (contraceptive transdermal patch); Elodose (low dose oral contraceptive); Topiramate (sprinkle and tablet antiepileptic); Levaquin (injectable and tablet antibiotic); Ultram (tablet analgesic, single and combination) and; Regranex (topical wound healing gel).

- Led the division through a staff reduction, put a high potential management team in place, and delivered improved performance based on use of metrics and deployment of process improvement methodologies.

- Initiated and managed a company-wide process improvement program spanning clinical and non-clinical development.

Assistant/Senior Director of Analytical Chemistry *(1991-1996)*
Held progressive levels of responsibility in management and leadership of analytical development. This department of 90 people provided all analytical chemistry support.

SmithKline Beecham | **1985-1991**
Various positions leading to Assistant Director, Pharmaceutical Analysis.

EDUCATION

*1985 - **Doctor of Philosophy, Analytical Chemistry**, Texas A&M University*

*1980 - **Bachelor of Arts, Chemistry**, Western Connecticut State University*

HONORS AND AWARDS - Sigma Xi, Phi Lambda Upsilon

PROFESSIONAL ACTIVITIES, COMMITTEES AND AWARDS

Honorary Advisor of the Sino American Pharmaceutical Association 1998-present
Pharmaceutical Research Manufacturer's Association, Analytical R&D Steering Committee 1995-1996

American Association of Pharmaceutical Scientists member since 1985 with service on Public Policy Committee 1994-1997

Adjunct Assistant Professor of Pharmaceutical Chemistry, University of Kansas, 1989-1992
American Chemical Society member since 1980, elected to Philadelphia Section Board of Directors 1986, participated on Continuing Education Subcommittee 1986-1990, Chaired 1989-1990

COMMUNITY ORGANIZATIONS

Delaware Township Community Education Foundation Board of Trustees, 1999-present, including Vice President of Science Committee 2000/1.

PUBLICATIONS AND PRESENTATIONS

Numerous with details available upon request.